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[Intervention Review]

Face washing promotion for preventing active trachoma

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ABSTRACT

Background

Trachoma remains a major cause of avoidable blindness among underprivileged populations in many developing countries. It is estimated that about 146 million people have active trachoma and nearly six million people are blind due to complications associated with repeat infections.

Objectives

The objective of this review was to assess the effects of face washing promotion for the prevention of active trachoma in endemic communities.

Search methods

We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (2015, Issue 1), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to January 2015), EMBASE (January 1980 to January 2015), PubMed (January 1948 to January 2015), Latin American and Caribbean Health Sciences Literature Database (LILACS) (January 1982 to January 2015), the *meta*Register of Controlled Trials (*m*RCT) (www.controlled-trials.com) (accessed 10 January 2014), ClinicalTrials.gov (www.clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 26 January 2015.

To identify further relevant trials we checked the reference lists of the included trials. Also, we used the Science Citation Index to search for references to publications that cited the trials included in the review. We contacted investigators and experts in the field to identify additional trials.

Selection criteria

We included randomized controlled trials (RCTs) or quasi-RCTs that compared face washing with no treatment or face washing combined with antibiotics against antibiotics alone. Trial participants were residents of endemic trachoma communities.

Data collection and analysis

Two review authors independently extracted data and assessed trial quality. We contacted trial authors for additional information when needed. Two trials met our inclusion criteria; but we did not conduct meta-analysis due to methodological heterogeneity.

Main results

We included two cluster-RCTs, which provided data from 2447 participants. Both trials were conducted in areas endemic to trachoma: Northern Australia and Tanzania. The follow-up period was three months in one trial and 12 months in the other; both trials had about 90% participant follow-up at final visit. Overall the quality of the evidence is uncertain due to the trials not reporting many design methods and the differences in outcomes reported between trials.

Face washing combined with topical tetracycline was compared with topical tetracycline alone in three pairs of villages in one trial. The trial found that face washing combined with topical tetracycline reduced 'severe' active trachoma compared with topical tetracycline alone at 12 months (adjusted odds ratio (OR) 0.62, 95% confidence interval (CI) 0.40 to 0.97); however, the trial did not find any important difference between the intervention and control villages in reducing other types of active trachoma (adjusted OR 0.81, 95% CI 0.42 to 1.59). Intervention villages had a higher prevalence of clean faces than the control villages among children with severe trachoma (adjusted OR 0.35, 95% CI 0.21 to 0.59) and any trachoma (adjusted OR 0.58, 95% CI 0.47 to 0.72) at 12 months follow-up. The second trial compared eye washing to no treatment or to topical tetracycline alone or to a combination of eye washing and tetracycline drops in children with follicular trachoma. At three months, the trial found no evidence of benefit of eye washing alone or in combination with tetracycline eye drops in reducing follicular trachoma amongst children with follicular trachoma (risk ratio (RR) 1.03, 95% CI 0.96 to 1.11; one trial, 1143 participants).

Authors' conclusions

There is evidence from one trial that face washing combined with topical tetracycline may be effective in reducing severe active trachoma and in increasing the prevalence of clean faces at one year follow-up. Current evidence is inconclusive as to the effectiveness of face washing alone or in combination with topical tetracycline in reducing active or severe trachoma.

PLAIN LANGUAGE SUMMARY

Face washing promotion for preventing active trachoma

Research question
We investigated whether face washing prevents active trachoma in endemic communities.

Background
Trachoma is an eye disease caused by bacterial infection. Active infection usually begins in childhood and is characterized by eye discharge, redness and irritation. Poor facial hygiene can lead to the disease spreading from person to person through eye-seeking flies or contaminated fingers. Face washing is promoted as part of the World Health Organization 'SAFE' strategy to eliminate blindness around the world. Face washing is simple and rational, but its effectiveness to reduce transmission of trachoma is uncertain.

Study characteristics
We included two randomized controlled trials with a total of 2560 participants set in Australia and Tanzania. One trial compared a combined strategy of face washing plus tetracycline (an antibiotic) ointment with tetracycline ointment alone for up to one year. The second trial compared four intervention groups for three months in children who already had follicular trachoma: a combined strategy of face washing plus tetracycline eye drops, face washing alone, tetracycline eye drops alone, and no treatment. The evidence is current to January 2015.

Key results
Both trials reported the number of children with active trachoma as an outcome measure; one trial also reported the number of children with severe trachoma and the percentage of clean faces after one year. One trial reported that face washing was effective in increasing facial cleanliness and in reducing severe trachoma at one year; the second trial did not show that eye washing alone or in combination with tetracycline eye drops reduced follicular trachoma amongst children who had follicular trachoma at time of enrollment.

Quality of evidence
The two included trials were of uncertain risk of bias due to not reporting many aspects of the trial designs.

BACKGROUND

Description of the condition

Trachoma is an infective eye disease caused by the bacterial microorganism *Chlamydia trachomatis*. Trachoma remains a major cause of avoidable blindness among underprivileged populations in many areas of Africa, Asia and the Middle East, where poverty, overcrowding, poor personal and environmental hygiene favor transmission of the disease. It is estimated that about 146 million people have active trachoma and nearly six million people are blind due to complications associated with repeat infections (WHO 1997a). *C. trachomatis* bacteria is spread from person to person by close contact in overcrowded living conditions, or through contaminated fingers or cloths used by mothers to wipe away discharges on the faces of children (ICEH 1999). Flies, which are attracted to eye and nasal secretions on the faces of infected children, also are believed to be vectors responsible for transmission of the organism (ICEH 1999; West 1991).

In communities where trachoma is endemic, infection usually begins in childhood and repeat episodes of infection cause distortion of the eyelids (entropion), in-turned eyelashes (trichiasis), corneal abrasion and ultimately blindness due to corneal opacity. Active trachoma is more commonly observed in children (Taylor 1985; West 1991). It is characterized by redness and discharge associated with inflammatory thickening of the upper tarsal conjunctiva (mucous membrane lining the inner surface of the upper eyelids) and follicles (whitish elevations within the conjunctiva). A simplified grading system for the assessment of trachoma and its complications in endemic communities has been published (Thylefors 1987) and discussed in a Cochrane review of antibiotics for trachoma (Evans 2011).

Description of the intervention

Face washing is promoted by the World Health Organization (WHO) program for the global elimination of trachoma as part of the 'SAFE' strategy (WHO 1997b; WHO 2011). The 'SAFE' strategy consists of **s**urgery for trichiasis; **a**ntibiotics for infectious trachoma; **f**acial cleanliness to reduce transmission; and **e**nvironmental improvements (household sanitation and provision of clean water).

How the intervention might work

The face washing component of the SAFE strategy aims to maintain clean faces in the community in order to reduce eye-seeking flies and person-to-person transmission of *C. trachomatis*. Face washing promotion as a community intervention can be combined with mass treatment of people with antibiotics in areas with high trachoma endemicity. Mass treatment with antibiotics aims to reduce the reservoir of *C. trachomatis* in the community, while face washing aims to interrupt the cycle of infection and re-infection in the long term. The antibiotic and environmental arms of the SAFE strategy have been examined in other published Cochrane reviews (Evans 2011; Rabiu 2012).

Why it is important to do this review

The face washing principle appears simple and theoretically sound, but whether this intervention can reduce transmission of trachoma in practice has been the focus of debate (Bailey 2001). Some narrative reviews of the literature have suggested that facial cleanliness may be useful in preventing trachoma (Emerson 2000; Pruss 2000). However, most of the data were obtained from observational studies and the methodological quality of the few controlled trials included was not reported. In this Cochrane review we aim to summarize systematically, research evidence from trials of face washing promotion for preventing active trachoma in endemic communities. In communities where water is scarce, the uptake and practice of face washing may not be as good as in communities where water is freely available. We will consider the potential influence of water availability on outcomes in this review.

OBJECTIVES

The objective of this review was to assess the effects of face washing promotion for the prevention of active trachoma in endemic communities.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomized controlled trials (RCTs) and quasi-RCTs.

Types of participants

Trial participants were residents of trachoma endemic communities.

Types of interventions

We considered the following interventions:

1. Face washing promotion versus no intervention;
2. Face washing promotion plus mass antibiotic treatment versus mass antibiotic treatment alone.

Face washing promotion can be delivered by any means appropriate to the local setting, such as: radio or television; health education leaflets; community leaders; religious gatherings; role-play; drama in village halls; school teachers; women groups; or music. In trials where promotion of face washing was combined with mass antibiotic treatment, antibiotics considered included tetracycline ointment or capsules, azithromycin, or erythromycin, given at any dose or frequency.

Types of outcome measures

We considered the following outcomes for comparison of interventions:

1. Number of participants with active trachoma (TF or TI) at 6, 12 or greater than 12 months post-treatment allocation (age group as reported in trials). We defined active trachoma using the Thylefors 1987 scale. On this scale, active trachoma is categorized as TF or TI. TF is trachoma follicular inflammation and is defined as the presence of five or more follicles, each of which is at least 0.5 mm in diameter, on the flat surface of the upper tarsal conjunctiva. TI is intense inflammation of the tarsal conjunctiva due to trachoma and is defined as the presence of marked inflammatory thickening of the upper tarsal conjunctiva that obscures more than half of the deep conjunctival vessels. We planned to include trials that used other trachoma grading scales to assess active trachoma, provided the scales used were comparable to the Thylefors 1987 scale;

2. Number of participants with an unclean face at 6, 12 or greater than 12 months post treatment allocation (age group as reported in trials). We defined an unclean face as the presence of eye or nasal discharge (WHO 2001) or any other definition used in trials;
3. Post hoc: Number of participants with severe trachoma. We did not specify severe trachoma among cases of active trachoma as an outcome in the protocol for this review (Ejere 2002). However, one of the two trials that met the inclusion criteria defined and reported this outcome.

Search methods for identification of studies

Electronic searches

We revised the searches of electronic databases from the 2012 update (Ejere 2012). We searched PubMed and the International Clinical Trials Registry Platform, which had not originally been searched. We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (2015, Issue 1), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily Update, Ovid OLDMEDLINE (January 1946 to January 2015), EMBASE (January 1980 to January 2015), PubMed (January 1948 to January 2015), Latin American and Caribbean Health Sciences Literature Database (LILACS) (January 1982 to January 2015), the *meta*Register of Controlled Trials (*m*RCT) (www.controlled-trials.com) (accessed 10 January 2014), ClinicalTrials.gov (www.clinicaltrial.gov), and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 26 January 2015.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), PubMed (Appendix 4), LILACS (Appendix 5), *m*RCT (Appendix 6), ClinicalTrials.gov (Appendix 7), ICTRP (Appendix 8).

Searching other resources

We contacted several trachoma experts, including Hedley Peach and Sheila West, to identify potentially relevant trials missed by the electronic searches. Denise Mabey was a peer reviewer and provided information on potentially relevant trials. We identified existing reviews and checked their citations for relevant trials. We used the Science Citation Index to search for references that cited the trials included in the review.

Data collection and analysis

Selection of studies

Two review authors independently screened titles and abstracts found through electronic searches. We retrieved the full-text of trials that were potentially relevant to the review. Those that met the selection criteria were assessed for methodological quality. We resolved any disagreements by discussion.

Data extraction and management

Two review authors independently extracted data onto a standardized data extraction form. We compared extracted data and reconciled differences. A third review author resolved any disagreements. We entered data into RevMan 2014. Where trials reported the outcomes in different ways, we contacted the primary investigators for further information to allow conversion or transformation of data.

Assessment of risk of bias in included studies

Two review authors independently assessed included trials using the following criteria based on Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Risk of bias domains assessed were selection bias (random sequence generation, allocation concealment before randomization), attrition bias (incomplete outcome data), reporting bias (selective outcome reporting) and other potential sources of bias. While masking of participants and intervention providers was not feasible due to the nature of the intervention of interest, masking of outcome assessors was possible and was assessed post hoc. We judged each included trial for each domain as being at "low", "unclear" "or "high" risk of bias and provided the rationale for each judgement. We provided direct quotes from included trials where appropriate.

Measures of treatment effect

The specified outcomes are dichotomous and therefore we calculated unadjusted risk ratios (RRs) with corresponding 95% confidence intervals (CIs). We also reported adjusted odds ratios (ORs) with corresponding 95% CIs as reported in the included trials.

Unit of analysis issues

Implementation of the intervention meant that clusters rather than individuals were randomized in the included trials. Cluster-RCTs should be analyzed on the same level as the allocation, using the summary measurement from each cluster, as opposed to the individual level measurement. Analyzing a cluster-RCT on the individual level could considerably and unnecessarily reduce the power of the trial.

Dealing with missing data

We contacted the trial authors in an effort to obtain missing outcome data or unclearly reported information, e.g. information about random sequence generation, allocation concealment or whether an intention-to-treat analyses was conducted.

Assessment of heterogeneity

We compared study designs and found methodological heterogeneity between the included trials that precluded meta-analysis of outcome data. If more trials are included in future updates of this review and we deem a meta-analysis appropriate, we will use the Chi^2 test to assess statistical heterogeneity but also will consider clinical and methodological heterogeneity of the included trials. Heterogeneity also may be apparent on visual examination of the forest plot.

Assessment of reporting biases

The trial protocol was not available for either included trial. If trial protocols of future included trials are available, we will compare reported outcomes with protocol-stated outcomes. When 10 or more trials are included in future updates of this review, we will use a funnel plot to display small study effects and potential for publication bias.

Data synthesis

We concluded that meta-analysis of the two included trials was not appropriate. However, if more trials are included in future updates and meta-analysis is appropriate, we will combine data using a random-effects model. When there are fewer than three trials and little evidence of heterogeneity, we will use a fixed-effect model. In meta-analyzing cluster-RCTs, when we encounter trials where the units of allocation and analysis are different (i.e. the unit of allocation was the community and the unit of analysis was individuals in the community) and the cluster design has not been accounted for in the analysis, we will contact primary investigators to obtain data required to develop estimates of intra-cluster correlation coefficients or design effects to calculate more appropriate CIs on effect estimates. Whenever a meta-analysis is not possible, we will present a tabulated summary of results.

Subgroup analysis and investigation of heterogeneity

We could not carry out subgroup analysis due to insufficient data. If more trials meet our inclusion criteria in an update of this review and we consider heterogeneity to be present, we will explore outcomes within the following subgroups:

1. Communities with available water supply versus communities with scarce water supply. We have defined water availability in this review as the presence of a functional water source within 30 minutes walk or a distance of less than 4 km from all households within the community (WHO 2001) or any other definition used in the trials;
2. Communities with intense active trachoma versus communities with less intense active trachoma. In this review we have defined intense active trachoma as communities with a baseline prevalence of TF or TI ≥ 20%, while less intense is defined as communities with a prevalence of TF or TI < 20% (WHO 1997b).

Sensitivity analysis

We could not perform sensitivity analysis as only two trials met our inclusion criteria. If a sufficient number of trials are included in future updates and a meta-analysis is appropriate, we plan to investigate the influence of trials with quasi-random methods and those without concealment of allocation on the pooled effect size. We also plan to measure the effect of publication bias on the pooled effect size. If feasible, we plan to assess whether the use of individual participant data would affect the direction of effect of interventions.

RESULTS

Description of studies

Results of the search

The original electronic searches in 2004 generated 67 citations and abstracts. We screened these results and retrieved the full text of two potentially relevant articles for further assessment. One of these met the criteria for inclusion (West 1995). The other was not a RCT and therefore excluded (Sutter 1983). A trachoma research expert drew our attention to a RCT that was not published in a journal (Peach 1987). Thus, we included two RCTs in the review.

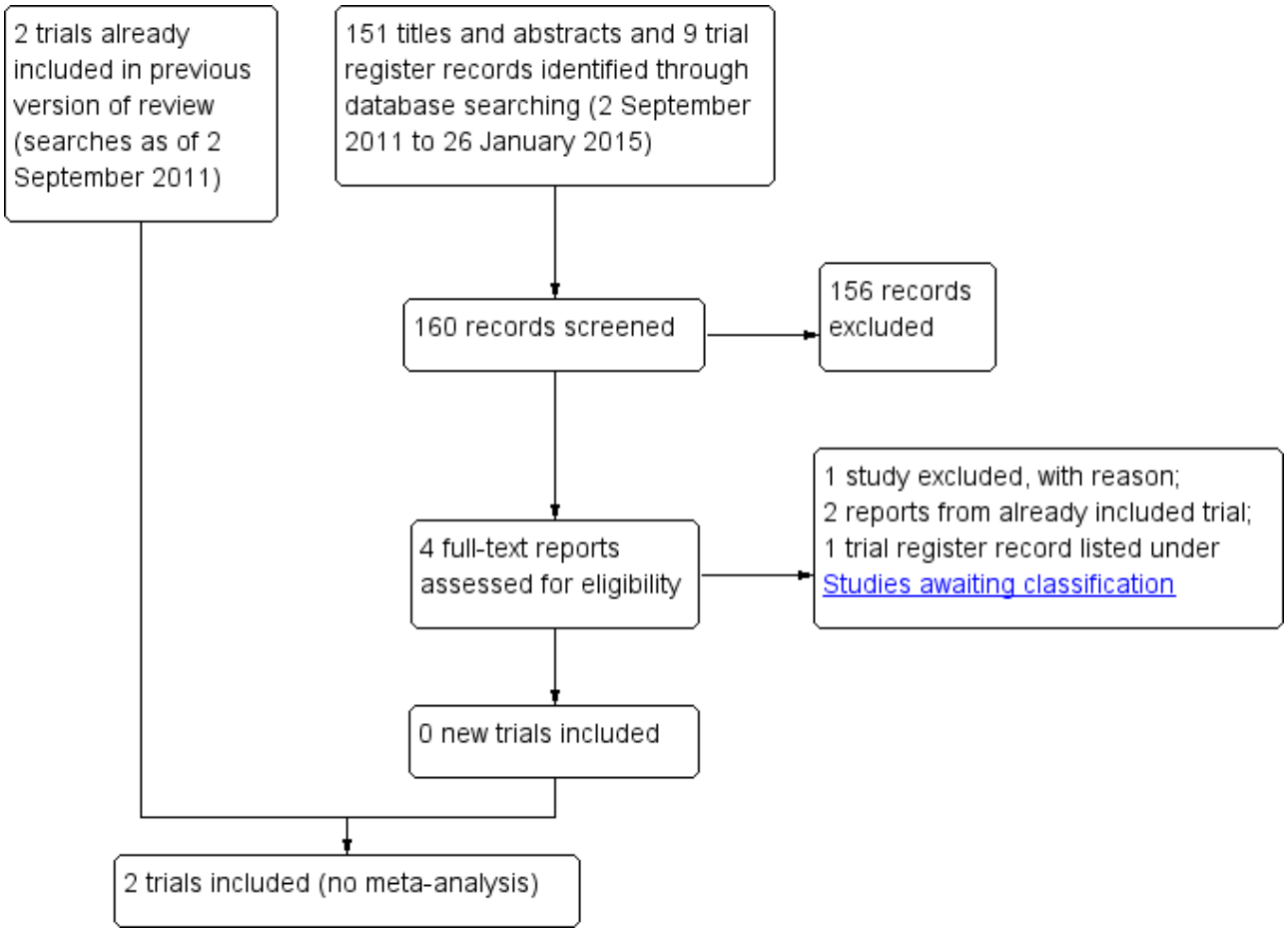
Updated searches

We performed a search in October 2007 and identified 66 new reports of trials. The Trials Search Co-ordinator scanned the search results and removed references she judged irrelevant to the scope of the review. We reviewed the full-text of three articles for potential inclusion; however, we excluded all three. Edwards 2006 and Rubinstein 2006 were reports of health education promotion of face washing and Khandekar 2006 treated face washing and environmental sanitation interventions as one outcome.

In September 2011 electronic searches identified 91 additional references. We assessed the full-text of one study (King 2011) but excluded it as it evaluated a standardized definition of a clean face for trachoma prevention.

In January 2015 we performed electronic searches and identified 151 additional titles and abstracts and nine trial register records (Figure 1). We classified three titles and abstracts and one trial register record to be potentially relevant and assessed the eligibility further based on the full-text reports. We excluded one study (Khandekar 2005) as it was not a RCT on face-washing promotion. Two other reports were from the West 1995 trial which we included in the previous version of the review. Under Characteristics of studies awaiting classification, we have described the trial register record (NCT00348478), which refers to a completed trial for which study results have not been published.

Figure 1. Study flow diagram.



Included studies

See Characteristics of included studies for further details.

Setting and participants

We included two cluster-RCTs (2560 children in total) conducted in areas endemic to trachoma. West 1995 was undertaken in Kongwa, Tanzania and included a total of 1417 children, aged one to seven years. Six villages were paired based on characteristics; one village of each pair was randomized to intervention and the other assigned to control. Peach 1987 was undertaken in the Northern Territory of Australia. In this trial 36 aboriginal communities were randomized to one of three intervention groups or one control group. A total of 2530 children aged five to 14 years were screened for follicular trachoma. Several children above the age of 14 years and some of preschool age were also screened. Of the total number of children screened in the participating communities, 1143 children with follicular trachoma were recruited into the trial.

Interventions

Both trials incorporated face washing as an intervention in the trial, but used different study designs and implementation methods. In West 1995, three villages (680 children) were randomized to face washing promotion combined with tetracycline and the three remaining villages (737 children) were assigned to tetracycline ointment alone. Face washing promotion was community-based and consisted of neighborhood meetings to build consensus for increasing face washing and reinforcement activities such as school plays, seminars with the traditional healers and meetings with other village groups. Face washing promotion was carried out for one month during and after mass treatment with tetracycline. Tetracycline ointment was administered topically once daily for 30 days.

In Peach 1987, 36 villages were randomized to either tetracycline eye drops (374 children), eye washing (246 children), eye washing combined with tetracycline eye drops (312 children) or no intervention (211 children). Children in the eye washing group had their eyes washed daily by school teachers for three months. Those in the tetracycline group had tetracycline eye drops applied daily for one week every month for three months. For the purpose of this review, we have reported data for the comparison between eye washing versus no treatment, and eye washing combined with eye drops versus eye drops alone.

Outcome measures

In West 1995, outcomes reported include active trachoma, severe trachoma and clean faces at 12 months. Trachoma was graded using the Thylefors 1987 scale. West 1995 defined severe trachoma as 15 or more follicles, or the presence of inflammation that obscured all vessels of the tarsal plate. We abstracted data from graphs presented in the report of the trial, as rates and raw data were unavailable. These abstracted data should be regarded as best approximations to the true figures. Our protocol specified

'unclean faces' as an outcome of interest, but West 1995 reported 'clean faces'. We elected to present the outcome as reported in the trial because it would be difficult to transform the data without sufficient information from the trialists.

In Peach 1987, the primary outcome was reported as the proportion of children with follicular trachoma at three months after the intervention. The Aboriginal Health Workers used a simplified grading scheme to assess the presence of follicles as indicating active trachoma. Although this scale is crudely comparable to the TF grading on the Thylefors 1987 scale, it may have a lower specificity because participants with fewer than five follicles may have been classified as having active trachoma.

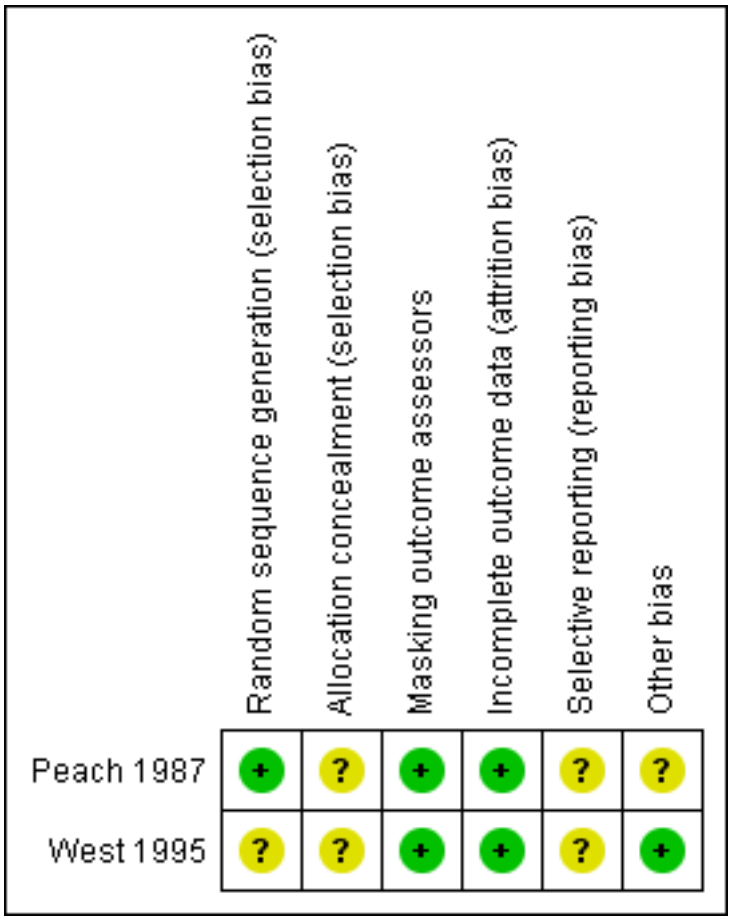
Excluded studies

See Characteristics of excluded studies for further details.

Risk of bias in included studies

Figure 2 gives the results of the assessment of methodological quality of the included trials.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

We assessed West 1995 at unclear risk of selection bias because no details of how randomization was performed or whether allocation assignments to intervention or control groups were concealed before randomization were reported. Authors of Peach 1987 stated that a random number table was used to allocate communities to an intervention or control group. Allocation was done after initial screening by someone who was unaware of the prevalence of trachoma and unfamiliar with the communities, including their school teachers and health workers, but no method of allocation concealment was reported. It is unclear whether baseline prevalence of trachoma was similar among the comparison groups. Information on the number of communities randomized to each experimental group was not available in the report. However, further correspondence with the trial authors suggested that about nine communities were randomized to each of the four trial groups.

Masking (performance bias and detection bias)

Masking of participants in West 1995 and Peach 1987 was not feasible. West 1995 masked outcome assessment by taking photographs of tarsal plates to be read by an examiner who was not aware of the randomization status of the villages. In Peach 1987, trachoma was assessed by trachoma workers who were unaware of treatment allocation to the communities. Steps were taken to ensure that the outcome assessors did not learn to which groups the communities were allocated. Different personnel carried out each intervention, namely eye washing and eye drops. School teachers washed the eyes of the children, while Aboriginal health workers or nurses administered eye drops. Since different

personnel carried out each intervention, workers could have become unmasked based on the presence or absence of certain personnel.

Incomplete outcome data

Incomplete outcome data was minimal for both trials. West 1995 reported baseline prevalences in active trachoma between comparison villages were not substantially different. Although 92% of the enrolled participants were followed up for one year, information regarding similarity of follow-up rates between comparison groups and handling of missing data was not reported.

In Peach 1987 89% of enrolled participants were followed up for three months. All participants lost to follow-up were assumed to have follicles at the end of the trial when the intention-to-treat principle was applied in the primary analysis of the results.

Selective reporting

Neither trial protocol was available for review.

Other potential sources of bias

Investigators in Peach 1987 controlled for observer variation and learning effect by allocating trachoma workers to all four groups in stages. Regardless, sensitivity and specificity among aboriginal trachoma workers in diagnosing follicular trachoma varied.

Effects of interventions

The two trials differed in several respects, particularly with regard to types of intervention, comparison group and definition of outcome measures. Therefore we did not consider a meta-analysis appropriate. We have presented a narrative summary of the results.

Active trachoma (follicular or TF or TI)

In West 1995, face washing combined with antibiotics was compared to antibiotics alone in three pairs of villages. In pair one, the percentage prevalence of active trachoma was reported to be lower in the village that received a combination of face washing and antibiotics than the village that received antibiotics alone at 12 months follow-up (approximately 55% compared to 60%; as read from figures; no numerical data provided for this pair or the other two pairs of villages). In a second pair of villages, the percentage of active trachoma also was lower in the combination intervention village than the antibiotics alone village (approximately 40% compared to 50%). However in a third pair of villages, the percentage of active trachoma in the combination intervention village was higher than the antibiotics alone village (approximately 70% compared to 65%). The overall results for all the combination intervention villages compared to the antibiotics alone villages suggest a reduction in the odds of any trachoma but this effect was not statistically significant (adjusted OR 0.81, 95% CI 0.42 to 1.59).

In Peach 1987, 191/246 children (77.6%) in the eye washing group had follicles at three months compared with 160/211 (75.8%) in the no treatment group (Analysis 1.1). The difference was not statistically significant (Analysis 1.1; RR 1.03, 95% CI 0.93 to 1.14). In the eye washing/eye drop combination group, 215/312 (68.9%) had follicles at three months compared to 250/374 (66.8%) in the eye drop only group. The difference was not statistically significant (Analysis 1.1; RR 1.02, 95% CI 0.93 to 1.13). When counting numbers of participants with presence of follicular trachoma, the trial investigators counted all missing cases as having follicular trachoma; the proportions of missing cases ranged from 9.0% to 17.9% among the four intervention groups.

When the Peach 1987 investigators fitted a logit model to the data to account for variations in participant age, geographical location and trachoma outcome assessors, the adjusted odds of having follicular trachoma were slightly higher in the eye drop only group compared to the eye washing/eye drop combination group (adjusted OR 1.17, 95% CI not reported). The adjusted odds of having follicular trachoma in the no treatment group compared to the eye washing group were similar and not statistically significant (adjusted OR 1.02, 95% CI not reported).

Severe trachoma

In West 1995 12-month prevalence of severe trachoma was compared between the intervention and control villages within each pair of villages. In pair one, the percentage prevalence of severe trachoma was lower in the village that received a combination of face washing and antibiotics than in the village that received antibiotics alone (approximately 8% compared to 14%). In a second pair of villages, the percentage of active trachoma also was lower in the combination intervention village than the antibiotic alone village (approximately 6% compared to 14%). However in the third pair of villages, the percentage of active trachoma in the combination intervention village was slightly higher than the antibiotics alone village (approximately 10% compared to 8%). The CIs and the numbers used to calculate these differences were not reported so that CIs of the differences could not be calculated. The overall results reported after adjustments for age and baseline trachoma status suggest a statistically significant reduction in the odds of severe trachoma by the face washing/antibiotics combination compared to antibiotics alone (adjusted OR 0.62, 95% CI 0.40 to 0.97). At six months follow-up, the trial authors reported that there was no difference in the prevalence of severe trachoma between the intervention and control groups in the three pairs of villages (data not provided).

Peach 1987 did not report this outcome.

Clean faces

In West 1995 the percentage of children with clean faces was consistently higher in the face washing-antibiotic combination villages than the antibiotic alone villages. Total results showed an increase in the percentage of children with clean faces in the face washing/antibiotic combination villages from 18% at baseline to 33% at six months and 35% at 12 months follow-up. There was a smaller increase in the percentage of children with clean faces in the antibiotic alone group (from 19% at baseline to 30% at six months and 26% at 12 months). The difference in the proportion of children with clean faces in the intervention villages compared to the control villages was statistically significant among those with severe trachoma (adjusted OR 0.35; 95% CI 0.21 to 0.59) and any trachoma (adjusted OR 0.58; 95% CI 0.47 to 0.72) at 12 months follow-up.

Peach 1987 did not report this outcome.

DISCUSSION

Summary of main results

Active trachoma

Two included trials reported active trachoma (defined as TF or TI with five or more follicles or inflammation obscuring at least half of tarsal conjunctiva vessels). The findings were either inconsistent within a trial or showed that the face washing/eye drop combination had no benefit.

It is unclear why face washing promotion combined with tetracycline had an effect on reducing active trachoma in two pairs of villages but no effect in a third pair in West 1995. Differences in baseline characteristics such as prevalence of trachoma, intensity of transmission, availability or access to water supplies between the third pair and the first two pair of villages may be important in explaining the differences in benefit. However, the overall results for the face washing/tetracycline combination villages compared to the tetracycline only villages suggest a modest, but not statistically significant, beneficial effect of face washing in reducing active trachoma at 12 months.

Peach 1987 suggested no benefit for face washing compared with no treatment or for the face washing/eye drops combination in comparison to eye drops alone. The age of participants varied, and there was a higher proportion of severe trachoma among older children. There were variations in the prevalence of trachoma in the different geographical locations from which the participating communities were drawn, as well as small differences in the diagnostic competence of outcome assessors. The trial authors hypothesized that community randomization in the trial may not have adequately controlled for these factors, hence the need to account for them. After fitting the data to a logit model to control for perceived imbalances in the ages of participants, geographical location and outcome assessors, a marginal but not statistically significant benefit was seen for the face washing/eye drops combination compared to the eye drops alone group. However, the report does not state whether the analysis of outcomes via logistic regression models was prespecified or post-hoc.

Severe trachoma (severe active trachoma)

Only West 1995 reported on severe trachoma (defined as TF or TI with more than 15 follicles or inflammation obscuring all the tarsal conjunctiva vessels). We refer to this outcome as "severe active trachoma". As for all active trachoma, the benefit of face washing in reducing the prevalence of severe trachoma was observed in two pairs of villages at 12 months follow-up, but not in the third pair. The reasons for this difference in outcome may have been due to differences in baseline characteristics of villages and participants, particularly the severity of trachoma at baseline.

Clean faces

West 1995 reported that the percentage of participants with clean faces increased in both intervention and control groups over 12 months, even though the increase was higher in the intervention group. However, a statistically significant difference in the percentage of clean faces between the intervention and control groups at 12 months suggests a benefit of face washing promotion.

Overall completeness and applicability of evidence

Although two trials are included in this review, we did not perform a meta-analysis because of clinical heterogeneity between the two trials, particularly with regard to intervention strategies and outcome definition. Although the reports of the design and conduct of the trials suggest that efforts were made by the investigators to assure high quality outcome data, lack of adequately reported information made it difficult to judge trial quality based on key quality parameters specified for this review (see Risk of bias in included studies and Figure 2). Peach 1987 reported outcomes at three months. Although the follow-up period fell short of what we specified in our protocol, we did not exclude the data from this trial in view of the paucity of RCTs. The two trials were conducted in Australia and Africa. Their generalizability to other countries and settings where trachoma is endemic is unknown.

Quality of the evidence

Active trachoma

If face washing indeed is beneficial with respect to active trachoma, the absence of an effect of face washing in Peach 1987 may be due to a number of factors. Firstly, the trachoma grading system used in the trial may have influenced the results. Participants were recruited into the trial on the basis of whether follicles or papillae were present. Children without trachoma who had follicles/papillae from other causes could have been included. For this group of children, treatment likely had no benefit. Furthermore, participants whose trachoma was less severe may not have experienced a benefit of face washing.

Secondly, in analyzing the results using the intention-to-treat principle, the trial authors assumed that all participants lost to follow-up had follicular trachoma at the end of the trial. If this assumption was incorrect and there were more participants lost to follow-up in a treatment group compared to control, as was the case with the eye washing group (17% versus 10.4%), treatment might appear to be ineffective compared with control. However, a sensitivity analysis with the missing participants excluded from analysis did not alter the result.

Thirdly, the intervention was administered for only three months. A longer intervention period and follow-up might have yielded different findings.

Fourthly, Peach 1987 applied face washing to children with established disease rather than the population at risk, and measured the outcome in this group of children. The face washing strategy aims to reduce active trachoma in endemic communities, mainly by reducing the transmission of the disease. The true impact of face washing on active trachoma in the communities might be better evaluated by a study design in which face washing is applied to whole populations at risk rather than only those with the disease and the number of new cases of disease since institution of the intervention determined. It is unclear how much impact on transmission can be achieved by applying face washing only to individuals in endemic communities who already have the disease.

Severe trachoma

The overall results of West 1995 for all the villages after adjusting for age and baseline trachoma status showed a benefit of face washing in reducing severe trachoma in the intervention villages

compared to the control villages at 12 months follow-up. It is probable that participants with severe active trachoma represent a subgroup with more intense transmission and therefore face washing, which aims to break transmission, would be more likely to show a stronger effect within this subgroup. On the other hand, the appropriateness of combining the results from the three pairs of villages is questionable, since presumably the villages were paired because of some differences among them. It is unclear why face washing showed no comparative benefit in the three pairs of villages at six months follow-up. Apparent benefit at 12 months underscores the importance of a longer follow-up period to ascertain the impact of the intervention.

Clean faces

The quality of evidence regarding the benefit of cleaning faces daily is largely unknown based on information available for the two included trials. Several methodological details were unreported or unclearly reported (allocation concealment, method of randomizations and attrition). There was inconsistency between the trials regarding the effect of clean faces on active trachoma.

Potential biases in the review process

We used a comprehensive search strategy in multiple databases, thus minimizing missed trials. There was no language restriction in the search for trials in order to reduce bias in locating eligible trials. The two included trials were conducted at least 20 years before this Cochrane review (reported in 1987 and 1995). We identified a completed but not yet reported study in our searches for eligible trials. Inclusion of findings from that study in our next review update may change our conclusions. We contacted trial authors for missing data and two review authors extracted data from the included trials.

Agreements and disagreements with other studies or reviews

A recent systematic review by Stocks 2014 showed a possible beneficial effect of clean faces in reducing the odds for active trachoma (TI/TF). Its objective was to "summarize the evidence in order to devise strategic and cost-effective approaches to trachoma prevention" (Stocks 2014). It included non-randomized studies that reported evidence showing that face washing at least once a day has an impact on both TF and TI (OR 0.76, 95% CI 0.57 to 0.96). It also showed that other hygiene-related exposures affect active trachoma (TI/TF), such as: ocular discharge, nasal discharge, soap use, bathing at least once a day and towel use. The methodological quality of the included studies was not addressed adequately in Stocks 2014.

AUTHORS' CONCLUSIONS

Implications for practice

Evidence from one trial suggests that face washing added to tetracycline eye drops can be effective in increasing facial cleanliness and in reducing severe trachoma during a 12-month period, but its effect in reducing active trachoma remains unknown. In the second trial, there was no evidence of a beneficial effect of face washing alone or in combination with tetracycline in reducing active trachoma in children with follicular trachoma.

Implications for research

The trials included in this review evaluated the effect of face washing over a three- to 12-month period. However, it is unclear whether this time period is long enough for a face washing promotional activity to demonstrate impact of the intervention. Therefore, if future research is continued in this area, longer follow-up periods should be used. Other areas for research would be to address the questions of whether reinforcement activities are required over time to improve outcome and the impact of better access to water in reducing trachoma. The reporting of the methodology of trials should be complete to enable reviewers and readers to assess the validity of their conclusions.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Peach 1987

Methods	**Study design:** cluster-RCT
	Number randomized: 36 communities (1143 children)
	Exclusions after randomization: none reported
	Unit of analysis: individual children
	Number analyzed: 1143 children total; 374 in eye drops group; 246 in eye washing group; 312 in combined group; 211 in non-treatment group
	Losses to follow-up: 128 (11.2%) children total; 34 in eye drops group; 44 in eye washing group; 28 in combined group; 22 in non-treatment group
	How was missing data handled?: "Children which the trachoma workers could not follow-up were assumed to have follicular trachoma and were included in the analysis."
	Reported power calculation: sample size of 1500; power 80%
	Unusual study design: "For each trachoma worker communities were allocated to all four groups and the allocation was done in stages…"

Peach 1987 *(Continued)*

Participants	**Country:** Northern Territory of Australia **Age:** 5 to 14 years; also included school children older than 14 years and pre-school children (ages not specified) **Gender:** boys and girls **Inclusion criteria for community:** Aboriginal communities in the Northern Territory; population of about 100 or more **Inclusion criteria for children:** Aboriginal children with follicular trachoma **Exclusion criteria for community:** communities where “the yield of trachoma cases was expected to be small (≤6)" **Equivalence of baseline characteristics:** no; "… more children aged 10 years old and above in the control group than in the other treatment groups …"
Interventions	**Intervention 1:** oily tetracycline eye drops daily for one week every month **Intervention 2:** daily (every school day) eye washing **Intervention 3:** oily tetracycline eye drops daily (every school day) for one week every month plus daily (every school day) eye washing **Intervention 4:** no treatment **Length of follow-up:** Planned: 3 months Actual: mean days of follow-up by intervention: 83.7 days for eye drops group, 85.6 days for eye washing group, 79.5 days for combined group, and 85.2 days for control group
Outcomes	**Primary outcome, as defined in trial reports:** follicular trachoma status (present or absent) **Secondary outcomes, as defined in trial reports:** none **Adverse events:** not reported **Intervals at which outcomes assessed:** baseline and 3 months
Notes	**Type of study:** published **Funding sources:** "The study was funded entirely by the Northern Territory Trachoma and Eye Health Committee Inc." **Disclosures of interest:** not reported **Study period:** not reported **Reported subgroup analyses:** yes (trachoma worker, geographical zone); "None of the differences between the trachoma workers in the results they obtained for any of the treatment programmes was statistically significant"; "The reduction in the number of children with follicular trachoma after the combined programme was significantly greater in communities in zones 2 and 8 than in zone 1." **Trial investigators contacted?:** yes; trial investigator contacted and provided information for previous versions of this review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A random number table was used to allocate communities to one of four treatment groups.

Peach 1987 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Allocation concealment not reported.
Masking outcome assessors	Low risk	"Trachoma workers did not know what treatment programme, if any, had been allocated to a particular community." "For each trachoma worker communities were allocated to all four groups and the allocation was done in stages to control for observer variation and a possible learning effect by the trachoma workers".
Incomplete outcome data (attrition bias) All outcomes	Low risk	128 (11.2%) children total (34 in eye drops group, 44 in eye washing group, 28 in combined group, 22 in non-treatment group) lost to follow-up; "The children whom the trachoma workers were unable to follow-up were assumed to have follicular trachoma and were included in the analysis… The data were re-analyzed after having excluded the missing cases and the overall results were similar"; "Level of missingness differed by treatment group – eye washing group had the highest % of missing cases".
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Unclear risk	This was a cluster-RCT; however, data were analyzed at the individual participant level without accounting for the cluster design; sensitivity and specificity of aboriginal trachoma workers in diagnosing follicular trachoma varied.

West 1995

Methods	**Study design:** cluster-RCT **Number randomized:** 6 villages (1417 children); villages paired so that one village was assigned to the intervention and the other assigned to control; Pair 1: 178 children in intervention village and 231 in control village; Pair 2: 248 children in intervention village and 247 in control village; Pair 3: 254 children in intervention village and 259 in control village; Total: 680 children in intervention group and 737 in control group **Exclusions after randomization:** none reported **Unit of analysis:** villages (overall and by pairs) **Number analyzed:** 6 villages **Losses to follow-up:** 113 children (8% of 1417); "reasons for loss to follow-up were that the child died (2%) or that the family moved out of the village or out of the study area (6%)" **How was missing data handled?:** not reported **Reported power calculation:** none **Unusual study design?:** pairs of villages matched for baseline characteristics; "We randomized three pairs of villages-one of each pair would receive mass treatment followed by the health education campaign, and the other would receive mass treatment alone. The pairs of villages were matched for maternal education (years of formal education), baseline prevalence of clean faces in young children, and trachoma status (based on clinical observation at enrolment). Within each village, a complete census was taken by trained field-workers. 250 eligible households containing at least 1 child aged 1-7 years

West 1995 *(Continued)*

	were randomly selected in each village. Within the household, 1 child was randomly selected to take part in the study."
Participants	**Country**: Kongwa, Tanzania **Age:** 1 to 7 years **Gender:** boys and girls **Inclusion criteria:** 1) children aged 1 to 7 years in the area where trachoma was endemic; 2) face washing campaign could be carried out at village level; 3) households containing at least 1 child **Exclusion criteria:** none reported **Equivalence of baseline characteristics:** no; pairs of villages were matched for maternal education, and baseline prevalence of clean faces in young children, and trachoma status based on clinical observation at enrolment; however, the prevalence of trachoma may have been higher in the intervention villages based on photographic evidence of trachoma
Interventions	**Intervention 1:** 30-day mass treatment campaign with topical tetracycline ointment once daily followed by intensive 1-month community-based participatory hygiene intervention, including neighborhood meetings and several reinforcement activities to improve face washing of the young children, during and after mass treatment **Intervention 2:** 30-day mass treatment campaign with topical tetracycline ointment once daily alone **Length of follow-up:** Planned: 12 months Actual: 12 months
Outcomes	**Outcomes, as defined in trial reports:** facial cleanliness based on the presence or absence of nasal discharge, ocular discharge, and flies on the face; trachoma status evaluated by photographs of the right eye of each index child graded on the WHO simplified grading scheme **Adverse events:** not reported **Intervals at which outcomes assessed:** baseline, month 2 (1 month after the end of the mass treatment campaign), 6 and 12 months
Notes	**Type of study:** published **Funding sources:** "This work was supported by the Edna McDonnell Clark Foundation and the Central Eye Health Foundation." **Disclosures of interest:** one author (Dr. Sheila West) is a Research to Prevent Blindness senior scientific investigator **Study period:** not reported **Reported subgroup analyses:** yes (trachoma status at baseline and prevalence of clean faces at baseline, 2 months, 6 months and 12 months) **Trial investigators contacted?:** yes; trial investigator contacted and provided information for previous versions of this review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomization not reported.

West 1995 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Allocation concealment not reported.
Masking outcome assessors	Low risk	"Records of facial cleanliness were made by trained observers who were not part of the hygiene intervention team." "At each time, the tarsal plate of the right eye of each index child was photographed. The photographs were graded on the WHO simplified grading scheme by one examiner who was unaware of the randomization status of the village and the time of the photograph."
Incomplete outcome data (attrition bias) All outcomes	Low risk	"92% were followed up for 1 year. The main reasons for loss to follow-up were that the child died (2%) or that the family moved out of the village or out of the study area (6%)."
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Low risk	No other sources of bias identified.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Edwards 2006	Face washing was not part of the study intervention. Communities were randomly assessed to different health education programs: 1. Radio messaging in 10 kebele not in the non-governmental organization (NGO) activity areas; 2. Radio messaging in 10 kebele within the NGO activity areas; 3. Radio messaging and information, education and communication (IEC) materials in 10 kebele within the NGO activity areas; 4. Radio messaging, IEC materials, and video van activities in 10 kebele within the NGO activity areas.
Khandekar 2005	Participants were not randomized to a face-washing program. Houses were randomly selected in communities where the face-washing "F" and education "E" components of the trachoma initiative were implemented.
Khandekar 2006	Unable to separate the effect of face washing from environmental sanitation interventions as both were indirectly examined as "one intervention".
King 2011	Study aim was to develop standardized definition for a clean face in trachoma prevention.
Rubinstein 2006	Study intervention is health education promotion of face washing; face washing was not part of the study intervention. The educational program had a primary and five secondary messages. The primary message is: "Eye disease can be prevented by washing children's faces with soap and water at least once each day." The secondary messages are: 1. Washing children’s faces with soap and water removes germs which can infect the eyes. 2. Eye disease can be reduced by always using latrines or burying human feces. 3. Eye disease can be reduced by burning or burying refuse such as food scraps and peelings from fruits and vegetables. 4. A dirty towel can carry infection from one child’s eyes to the eyes of another child. 5. Anything that touches eyes, including hands, can spread eye infections.
Sutter 1983	Not a RCT; communities were not randomly assigned care groups. Care groups are villages who are involved in prevention and treatment of trachoma.

Characteristics of studies awaiting assessment *[ordered by study ID]*

NCT00348478

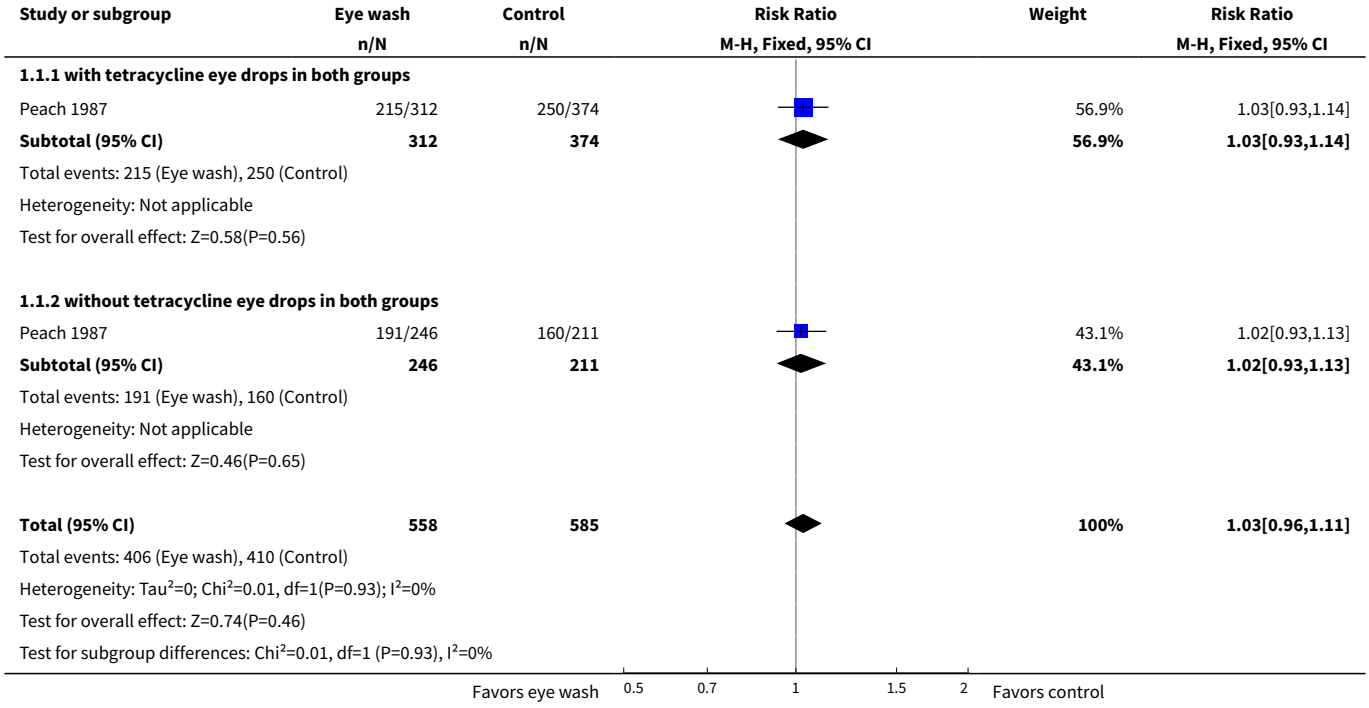
Methods	**Study design:** cluster-RCT **Unit of randomization:** villages. "We will randomly select six villages to be the "intervention" villages and six villages to be the "control" villages. We will aim to include 360 children, randomly selected from the 6 "intervention" villages (one per mother for a total of up to 60 in each village) and 360 children randomly selected from 6 "control" villages."
Participants	**Country:** Niger **Age:** 6 months to 5 years and five months **Gender:** boys and girls **Inclusion criteria:** villages of size between 900 to 2100 residents as of 1995 census in Kornaka West district of Niger; village leadership approval of entry of village in the study; sentinel children ages 6 months to 5 years and five months **Exclusion criteria:** village already has health education program for hygiene; village within 5 km of a well; child already has a sibling in the study population
Interventions	**Intervention 1:** water and health education program to improve hygiene; "World Vision plans water wells to serve a population of about 300, in villages of about 300-5,000 persons. Thus each village has around 1-17 wells. The goal is to provide water within 500 meters with a wait time of less than 15 minutes. Health education on use of water and hygiene practices is also part of services delivery. A World Vision Area Development Program officer establishes and trains a water and sanitation committee to provide health education for their village." **Intervention 2:** "control" villages where services not available immediately; "villages where the planning process has just started and wells would not be drilled for over two years" **Length of follow-up:** Planned: 3 years
Outcomes	**Primary outcome, as defined in trial:** trachoma (ocular *C. trachomatis* infection) **Secondary outcome, as defined in trial:** under five years **Adverse events:** not specified **Intervals at which outcomes assessed:** baseline, 1, 2, and 3 years from baseline
Notes	**Type of study:** unpublished **Funding sources:** Johns Hopkins University, World Vision, CONRAD **Disclosures of interest:** not reported **Study period:** not reported **Planned subgroup analyses:** none reported

DATA AND ANALYSES

Comparison 1. Eye wash versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Presence of follicular trachoma	1	1143	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.96, 1.11]
1.1 with tetracycline eye drops in both groups	1	686	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.93, 1.14]
1.2 without tetracycline eye drops in both groups	1	457	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.93, 1.13]

Analysis 1.1. Comparison 1 Eye wash versus control, Outcome 1 Presence of follicular trachoma.



APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Trachoma] explode all trees
#2 MeSH descriptor: [Chlamydia trachomatis] explode all trees
#3 trachom* or tracom*
#4 (follicular near/3 conjunctivitis)
#5 (intense near/3 conjunctivitis)
#6 Egyptian Ophthalmia*
#7 (Chlamydia* near/3 conjunctivitis)
#8 (granular near/3 conjunctivitis)
#9 (chlamydiasis or chlamidiosis)

#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #9
#11 MeSH descriptor: [Hygiene] explode all trees
#12 MeSH descriptor: [Face] explode all trees
#13 face* near/3 (wash* or clean* or hygien*)
#14 facial near/3 (wash* or clean* or hygien*)
#15 #11 or #12 or #13 or #14
#16 #10 and #15

Appendix 2. MEDLINE (OvidSP) search strategy

1. Randomized Controlled Trial.pt.
2. Controlled Clinical Trial.pt.
3. (randomized or randomised).ab,ti.
4. placebo.ab,ti.
5. drug therapy.fs.
6. randomly.ab,ti.
7. trial.ab,ti.
8. groups.ab,ti.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. exp animals/ not humans.sh.
11. 9 not 10
12. exp Trachoma/
13. exp Chlamydia trachomatis/
14. trac?oma$.tw.
15. (follicular adj3 conjunctivitis).tw.
16. (intense adj3 conjunctivitis).tw.
17. Egyptian Ophthalmia$.tw.
18. ((Chlamydia$ adj3 conjunctivitis) or (granular adj3 conjunctivitis)).tw.
19. (chlamydiasis or chlamidiosis).tw.
20. 12 or 13 or 14 or 15 or 16 or 17 or 18
21. exp Hygiene/
22. exp Face/
23. (face$ adj3 (wash$ or clean$ or hygien$)).tw.
24. (facial adj3 (wash$ or clean$ or hygien$)).tw.
25. 21 or 22 or 23 or 24
26. 20 and 25
27. 11 and 26

The search filter for trials at the beginning of the strategy is adapted from the published paper by Glanville et al (Glanville 2006).

Appendix 3. EMBASE.com search strategy

#1 'randomized controlled trial'/exp
#2 'randomization'/exp
#3 'double blind procedure'/exp
#4 'single blind procedure'/exp
#5 random*:ab,ti
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 'animal'/exp OR 'animal experiment'/exp
#8 'human'/exp
#9 #7 AND #8
#10 #7 NOT #9
#11 #6 NOT #10
#12 'clinical trial'/exp
#13 (clin* NEAR/3 trial*):ab,ti
#14 ((singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*)):ab,ti
#15 'placebo'/exp
#16 placebo*:ab,ti
#17 random*:ab,ti
#18 'experimental design'/exp
#19 'crossover procedure'/exp
#20 'control group'/exp
#21 'latin square design'/exp

#22 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#23 #22 NOT #10
#24 #23 NOT #11
#25 'comparative study'/exp
#26 'evaluation'/exp
#27 'prospective study'/exp
#28 control*:ab,ti OR prospectiv*:ab,ti OR volunteer*:ab,ti
#29 #25 OR #26 OR #27 OR #28
#30 #29 NOT #10
#31 #30 NOT (#11 OR #23)
#32 #11 OR #24 OR #31
#33 'trachoma'/exp
#34 'chlamydia trachomatis'/exp
#35 'chlamydiasis'/exp
#36 trachoma*:ab,ti OR tracoma*:ab,ti
#37 (egyptian NEAR/1 ophthalmia*):ab,ti
#38 (chlamydia* NEAR/3 conjunctivitis):ab,ti OR (granular NEAR/3 conjunctivitis):ab,ti
#39 chlamydiasis:ab,ti OR chlamidiosis:ab,ti
#40 (follicular NEAR/3 conjunctivitis):ab,ti
#41 (intense NEAR/3 conjunctivitis):ab,ti
#42 #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41
#43 'personal hygiene'/exp
#44 'face'/exp
#45 (face* NEAR/3 (wash* OR clean* OR hygien*)):ab,ti
#46 (facial NEAR/3 (wash* OR clean* OR hygien*)):ab,ti
#47 #43 OR #44 OR #45 OR #46
#48 #32 AND #42 AND #47

Appendix 4. PubMed search strategy

#1 ((randomized controlled trial[pt]) OR (controlled clinical trial[pt]) OR (randomised[tiab] OR randomized[tiab]) OR (placebo[tiab]) OR (drug therapy[sh]) OR (randomly[tiab]) OR (trial[tiab]) OR (groups[tiab])) NOT (animals[mh] NOT humans[mh])
#2 (trachoma*[tw] OR tracoma*[tw]) NOT Medline[sb]
#3 (follicular[tw] AND conjunctivitis[tw]) NOT Medline[sb]
#4 (intense[tw] AND conjunctivitis[tw]) NOT Medline[sb]
#5 Egyptian Ophthalmia*[tw] NOT Medline[sb]
#6 (chlamydia*[tw] AND conjunctivitis[tw]) NOT Medline[sb]
#7 (granular[tw] AND conjunctivitis[tw]) NOT Medline[sb]
#8 (chlamydiasis[tw] OR chlamidiosis[tw]) NOT Medline[sb]
#9 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10 (face*[tw] AND (wash*[tw] OR clean*[tw] OR hygien*[tw])) NOT Medline[sb]
#11 (facial AND (wash*[tw] OR clean*[tw] OR hygien*[tw])) NOT Medline[sb]
#12 #10 OR #11 OR #12
#13 #9 AND #12
#14 #1 AND #13

Appendix 5. LILACS search strategy

(Trachoma OR Tracoma OR "Egyptian Ophthalmia" OR MH:C01.252.354.225.800$ OR MH:C01.252.400.210.210.800$ OR MH:C01.539.375.354.220.800$ OR MH:C11.187.183.220.889$ OR MH:C11.204.813$ OR MH:C11.294.354.220.800$ OR MH:C23.996.850$ OR "Chlamydia trachomatis" OR MH:B03.440.190.190.190.750$ OR Chlamydia$ conjunctivitis OR "granular conjunctivitis" OR chlamydiasis OR chlamidiosis OR "follicular conjunctivitis" OR "intense conjunctivitis") AND (MH:E02.547$ OR MH:N06.850.670$ OR MH:SP4.001.017.193$ OR MH:A01.456.505$ OR ((Face$ OR Cara$ OR facial$) AND (wash$ OR clean$ OR Higien$ OR Hygien$)))

Appendix 6. *meta*Register of Controlled Trials search strategy

(wash or clean or hygiene) and trachoma

Appendix 7. ClinicalTrials.gov search strategy

(wash OR clean OR hygiene) AND trachoma

Appendix 8. ICTRP search strategy

trachoma AND wash OR trachoma AND clean OR trachoma AND hygiene

WHAT'S NEW

Date	Event	Description
17 February 2015	New citation required but conclusions have not changed	Issue 2, 2015: Text of review has been updated/re-organised using subheadings
17 February 2015	New search has been performed	Issue 2, 2015: Updated searches yielded no new studies for inclusion.

HISTORY

Protocol first published: Issue 2, 2002
Review first published: Issue 3, 2004

Date	Event	Description
3 February 2012	New search has been performed	Issue 4, 2012: Updated searches yielded no new studies for inclusion.
3 February 2012	New citation required but conclusions have not changed	Issue 4, 2012: Risk of bias assessment has been amended to reflect updated changes by The Cochrane Collaboration.
23 October 2008	Amended	Converted to new review format.
20 February 2008	New search has been performed	Issue 2 2008: three new trials were identified in an updated search but were excluded.
31 March 2004	New citation required and conclusions have changed	Substantive amendment.

CONTRIBUTIONS OF AUTHORS

HE conceived, coordinated, screened search results, organized retrieval of papers, screened retrieved papers against inclusion criteria, appraised risk of bias and abstracted data, wrote to authors of papers for additional information, entered data into RevMan 2014, interpreted data, and wrote the review.

MA screened search results, screened retrieved papers against inclusion criteria, appraised risk of bias and abstracted data, and wrote the review.

MR screened retrieved papers against inclusion criteria, appraised risk of bias and abstracted data, resolved disagreements between reviewers, interpreted the data, and wrote the review.

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HE: none known.
MA: none known.
MR: none known.

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  The views expressed in this publication are those of the authors and not necessarily those of the NIHR, NHS, or the Department of Health.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We did not specify severe trachoma among cases of active trachoma as an outcome in the protocol for this review (Ejere 2002). However, one of the two trials that met the inclusion criteria defined and reported this outcome; thus, we have included these results.

We revised the searches of electronic databases to include PubMed and the International Clinical Trials Registry Platform, which had not originally been searched.

INDEX TERMS

Medical Subject Headings (MeSH)

*Face; Anti-Bacterial Agents [administration & dosage]; Australia; Baths [*methods]; Chlamydia trachomatis; Combined Modality Therapy [methods]; Ophthalmic Solutions [therapeutic use]; Randomized Controlled Trials as Topic; Skin Care [*methods]; Tanzania; Tetracycline [administration & dosage]; Trachoma [epidemiology] [*prevention & control]

MeSH check words

Adolescent; Child; Child, Preschool; Humans; Infant